**Supplementary Methods**

**Circulating PBMC surface staining and flow cytometry**

For phenotypic analysis of Tfh, Th1, Th2 and Th17 cells, freshly isolated PBMC were stained with the following fluorochrome conjugated antibodies: CD183-PerCPCy5.5, CXCR5-AF647, PD-1-PE, CD45RA-FITC, CD196-PECy7 (all BD Biosciences, San Jose, CA), CD4-Vio Blue (Miltenyi Biotec, San Diego, CA), and NIR LIVE/DEAD dye (Life Technologies, Carlsbad, CA). Tfh cells were gated as CD4+CD45RA-CXCR5+ cells. These cells were further gated to define CXCR3+CCR6- Tfh1 cells, CXCR3-CCR6- Tfh2 and CXCR3-CCR6+ Tfh17 subsets. Flow cytometry was performed using MACSQuant (Miltenyi Biotec, San Diego, CA) and data were analysed using FlowJov10.0 (TreeStar, Ashland, OR).

**Tfh cell and B cell isolation and co-culture assay**

Fresh PBMC were enriched for CD4+ T-cells by negative selection using magnetic beads according to manufacturer’s instructions (StemCell Technologies, Vancouver, Canada). Enriched CD4+ cells were surface stained with CXCR5-AF647, PD1-PE, CD45RA-FITC, CD4-VioBlue (all BD Biosciences, San Jose, CA), NIR LIVE/DEAD dye (Life Technologies, Carlsbad, CA). Cell sorting for CD45RA- CD4+CXCR5+PD1+and CD45RA-CD4+CXCR5+PD1- Tfh cells was performed using MoFlo (XDP–Beckman Coulter, Brea, CA). To obtain B cells, fresh PBMC were enriched by positive magnetic bead selection for CD27+B-cells according to manufacturer’s instructions (Miltenyi Biotech, San Diego, CA).

B cells (3 x 104 cells/well) were co-cultured with PD1+ or PD1- Tfh cells (3x104 cells/well) in a 1:1 ratio in AIM-V medium (Life Technologies, Carlsbad, CA). Cells were stimulated with staphylococcal enterotoxin B (SEB, 100ng/ml, Sigma-Aldrich, St. Louis, MO). After 7-days supernatants were removed and frozen. Co-cultured cells were surface stained with CD38-PerCPCy5.5, CD27-PECy7 (both BD Biosciences, San Jose, CA), CD19-Pacific Blue (BioLegend, San Diego, CA), CD20-Pacific Orange (Life Technologies, Carlsbad, CA) and NIR LIVE/DEAD dye (Life Technologies, Carlsbad, CA) to identify antibody secreting cells. To evaluate cell proliferation, cultured cells were surface stained with CD4-Vio Blue (Miltenyi Biotec, San Diego, CA) and NIR LIVE/DEAD dye (Invitrogen Life Technologies, Carlsbad, CA) and then fixed, permeabilised and stained with Ki67-FITC (BD Biosciences, San Jose, CA) using FoxP3/Transcription Factor Staining Buffer Set (eBioscience, San Diego, CA).

**IgG4 ELISA**

ELISA plates were coated with anti-IgG4 (MH164-1, Sanquin Reagents, Amsterdam,) in PBS and stored overnight at room temperature (RT). After washing in 0.02% PBS-Tween, the culture supernatants harvested on day-7 were added to the plate and shaken at RT for 2 hours. After washing in 0.02% PBS-Tween, horseradish peroxidase conjugated-mouse-anti-human-IgG (MH16-1, Sanquin Reagents, Amsterdam) was applied to the plate and shaken at RT for 1 hour. Plates were developed with tetramethylbenzidine substrate (Sigma-Aldrich, St. Louis, MO) and 1M H2SO4 was used to stop the reaction. Absorption was measured at 450nm using a SpectraMax340 Plate reader (Molecular Devices, UK Ltd).

**Cytokine Immunoassays**

B cell and plasmablast culture supernatants were analysed for cytokines IL-4, IL-5, IL-10, IL-13, IL-17A, IL-21, B-cell activating factor (BAFF) and Transforming growth factor beta (TGFβ) using quantitative multiplexed immunoassay based on Luminex technology, using a Procarta immunoassay kit (Affymetrix). In brief, two 96-well filter plates were prepared by incubating with 150μl of Reading buffer (containing sodium azide) for 5 mins at RT. 50μl of antibody polystyrene beads were added to each well, then washed once. Plates were analysed on a calibrated Luminex instrument, detecting both low and high RP1 target values. The concentrations of the samples were calculated by plotting expected concentrations of standards against the MFI generated by each standard.

Tfh and B cell co-culture supernatants were analysed for the presence of IL-10, IL-21, IL-17A and IL-4 cytokines using Milliplex Map Human Th17 Magnetic Bead Panel according to manufacturer’s instructions (Merck Millipore, Billerica, MA). Plates were read using BioRad Bio-Plex Manager Software, version 6 (BioRad, Hercules, CA).

**Histological staining**

Tissues were stained for CD4 T-cells (Clone 4B12, Dako, UK), CXCR5 Tfh cell marker (Abcam, Cambridge), ICOS activation marker (Clone ab105227, Abcam, Cambridge), and CXCL13 (Clone 53610, R&D Systems, Minneapolis, USA), a chemokine ligand important in homing of B cells in lymphoid tissue and implicated in the formation of ectopic lymphoid tissue in chronic inflammation. In brief, 4 micro-meter (µm) paraffin sections were cut from selected blocks and mounted onto coated slides (Thermofisher Scientific), which were dried for 20 minutes at 60oC. Slides for immunohistochemistry were prepared using the automated Prepstain Detection-system (Dako-Cytomation, Hamburg, Germany). Staining utilised the Dako Medical Systems System with peroxidase and diaminobenzidine (DAB) solution containing 0.05% hydrogen peroxide for visualisation. Interpretation of cellular staining was performed by two observers, using a multi-headed microscope to agree scores (ACB and ELC). The absolute number of cells expressing each marker per high power field (HPF) was counted, and an average of three HPF was recorded. The intensity of immunostaining was semi-quantitatively evaluated and scored as absent = 0; few = +; moderate = ++; abundant = +++.

**Statistical Analysis**

Prism 6.0 (GraphPad, La Jolla, CA) was used for statistical analyses. Comparisons between two datasets were made using the Mann-Whitney U non-parametric test for unpaired data and Wilcoxon signed rank test for paired data, and between multiple variables by two-way ANOVA with multiple comparisons. Multiple regression analysis was performed where there was more than one explanatory variable. Chi Squared or Fishers Exact test were used for categorical variables. Pearson’s correlation and Spearman’s correlation coefficients were used for parameters with a Gaussian and non-Gaussian distribution, respectively. A p-value <0.05 was considered statistically significant.